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(FILE 'USPAT' ENTERED AT 14:57:25 ON 11 SEP 1998)

L1 1 S 5447851/PN  
L2 1 S 5731168/PN  
L3 101 S FC(5A) (FUSION OR CHIMER?)  
L4 66 S L3(P) (IG?)  
L5 1 S 5395760/PN  
L6 0 S L5 AND (DIMER? OR MULTIMER?)  
L7 1 S L5 AND FUSION?  
L8 31925 S DIMER? OR MULTIMER? OR HETEROMULTIM? OR HOMOMULTIM?  
L9 1392 S L8(6A) (PROTEIN? OR POLYPEPTID? OR RECEPTOR?)  
L10 2024 S L8/AB OR L8/CLMS  
L11 82 S L10(6A) (PROTEIN? OR POLYPEPTID? OR RECEPTOR?)  
L12 81 S L11 NOT L4

5,116,964 -16  
+3  
5,428,130 1.2  
-9  
5,714,477 2

*Late*

US PAT NO: 5,605,690 [IMAGE AVAILABLE] L4: 48 of 66  
DATE ISSUED: Feb. 25, 1997  
TITLE: Methods of lowering active TNF-.alpha. levels in mammals  
using tumor necrosis factor receptor  
INVENTOR: Cindy A. Jacobs, Seattle, WA  
Craig A. Smith, Seattle, WA  
ASSIGNEE: Immunex Corporation, Seattle, WA (U.S. corp.)  
APPL-NO: 08/385,229  
DATE FILED: Feb. 8, 1995  
REL-US-DATA: Continuation of Ser. No. 946,236, Sep. 15, 1992,  
abandoned, which is a continuation-in-part of Ser. No.  
523,635, May 10, 1990, Pat. No. 5,395,760, which is a  
continuation-in-part of Ser. No. 421,417, Oct. 13, 1989,  
abandoned, which is a continuation-in-part of Ser. No.  
405,370, Sep. 11, 1989, abandoned, which is a  
continuation-in-part of Ser. No. 403,241, Sep. 5, 1989,  
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INT-CL: [6] A61K 39/395; A61K 38/00; C12P 21/04; C07K 14/715  
US-CL-ISSUED: 424/134.1; 435/69.7; 514/12, 825; 530/350, 387.3, 866, 868  
US-CL-CURRENT: 424/134.1; 435/69.7; 514/12, 825; 530/350, 387.3, 866, 868  
SEARCH-FLD: 435/69.1, 69.7, 172.3, 240.27; 424/85.1, 134.1; 530/351,  
387.3, 868; 935/9, 12, 15

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ART-UNIT: 186  
PRIM-EXMR: Lila Feisee  
ASST-EXMR: John Lucas  
LEGAL-REP: Stephen L. Malaska

ABSTRACT:

A method for treating TNF-dependent inflammatory diseases in a mammal by  
administering a TNF antagonist, such as soluble TNFR.  
6 Claims, 7 Drawing Figures

## DRAWING DESC:

DRWD(2)

FIG. 1 shows the dimeric structure of the recombinant human TNFR/**Fc fusion** protein. The primary translation product of the plasmid coding for rhu TNFR/Fc is a single molecule of soluble TNFR linked to single chain of Fc derived from human **IgG1**. Following translation, but prior to secretion, this fusion molecule dimerizes via 3 cysteine residues in the Fc region to form. . .

## DETDESC:

DETD(24)

A . . . either or both of the immunoglobulin molecule heavy and light chains and having unmodified constant region domains. For example, chimeric TNFR/**IgG**.sub.1 may be produced from two chimeric genes--a TNFR/human .kappa. light chain chimera (TNFR/G.sub..kappa.) and a TNFR/human .gamma..sub.1 heavy chain chimera. . . displayed bivalently. Such polyvalent forms of TNFR may have enhanced binding affinity for TNF ligand. One specific example of a TNFR/**Fc fusion** protein is disclosed in SEQ ID NO:3 and SEQ ID NO:4. Additional details relating to the construction of such chimeric. . .